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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/747,514	12/21/2000	Paul V. Phibbs	5218.87	1007

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MYERS BIGEL SIBLEY & SAJOVEC
PO BOX 37428
RALEIGH, NC 27627

EXAMINER
GIBBS, TERRA C

ART UNIT	PAPER NUMBER
1635	11

DATE MAILED: 03/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/747,514	PHIBBS ET AL.	
	Examiner	Art Unit	
	Terra C. Gibbs	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-9 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-9 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's Amendment, filed on 12/23/02, in Paper No. 10 is acknowledged.

Claims 10-15 have been canceled.

Claims 1-9 are pending in the instant application.

Specification

The Amendment to the Abstract of the Disclosure, filed on 12/23/02, to contain clear and concise language is acknowledged. However, this Amendment does not overcome the instant objection to the Specification. Again, Applicant is reminded of the proper language and format for an Abstract of the Disclosure.

The Abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the Abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "**said**," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "**said bacteria**".

Information Disclosure Statement

The Information Disclosure Statement, filed 8/29/02, in Paper No. 8 is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The term "combinatorial library" in claim 8 is a relative term which renders the claim indefinite. The term "combinatorial library" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Clarification is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1 and 2 are drawn to a method of screening for compounds that inhibit the virulence of *Pseudomonas* bacteria, comprising providing a culture medium comprising *Pseudomonas* bacteria; administering a test compound to the bacteria and detecting the presence or absence of inhibition of the catabolite repression control (Crc) protein;

wherein the *Pseudomonas* bacteria is selected from the group consisting of *Pseudomonas aeruginosa*, *Pseudomonas multivorans*, *Pseudomonas fluorescens* and *Pseudomonas putida*. Claims 4 is dependent on claim 1 and includes all the limitations of claim 1; wherein the culture medium contains an amidase operon repressor and fluoroacetamide and the detecting step is carried out by detecting the poisoning of the bacteria by fluoroacetamide; wherein the poisoning of the bacteria by the fluoroacetamide indicates the test compound has antivirulence activity against *Pseudomonas* bacteria. Claims 5-7 are dependent on claim 4 and include all the limitations of claim 4; wherein the amidase operon repressor is selected from the group consisting of Krebs cycle intermediates and acetate; wherein the amidase operon repressor is succinic acid; wherein the step of detecting the poisoning of the bacteria is carried out by detecting cell death or inhibition of cell growth. Claims 8 and 9 are dependent on claim 1 and include all the limitations of claim 1, wherein the test compound is a member of a combinatorial library; wherein the test compound is an oligonucleotide.

The instant specification, at page 4, lines 27-31, discuss test compounds, including combinatorial libraries of such compounds, that may be screened for activity by the methods of the invention are, in general, small organic compounds (i.e. non-oligomers), oligomers, or combinations thereof. Compounds which exhibit activity in these methods are referred to as "active compound". The instant specification, at page 6, lines 23-26, defines "active compounds" as compounds that exhibit antivirulence activity in the screening procedures in the screening procedures described above. Such compounds may be oligomers (including antisense oligonucleotides) or nonoligomers.

The instant claims read on a test compound, where the test compound has been described as small organic compounds (i.e. non-oligomers), oligomers, or combinations thereof.

The claimed invention encompasses any test compound, where the test compound is any small organic compound, any oligomer, or any combination thereof.

The specification, at page 5, lines 1-9, describes general small organic compounds (non-oligomers). The specification provides an example of oligonucleotides as SEQ ID NOs. 1, 2, 3 and 4 (see specification page 5, lines 21-22). However, the specification as filed, does not provide sufficient description that would allow one of skill in the art to use NOs. 1, 2, 3 and 4 to predict the structures of any oligomer, or any combination thereof that would act as a test compound in the instant invention.

The specification fails to describe the complete structure of a representative number of species of the claimed genus. See the Guidelines for Examination of Patent Applications Under the 35 USC 112 ¶ 1, "Written Description" Requirement (Vol. 66, No. 4, pages 1099-1111). These guidelines state that: "To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the

invention was complete, or by describing distinguishing identifying characteristics sufficient to show that applicant was in possession of the claimed invention." In the instant case, the specification does not describe or identify characteristics that can be used to distinguish species of the claimed genus.

Additionally, "[T]he skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence."

Applicant's specification does not provide a sufficient number of representative species test compounds, where the test compounds are any oligomer, or any combination thereof, which would allow one of skill in the art to predict the structures of all members of the claimed genus of compounds. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Therefore, the specification does not describe the claimed compounds in such full and concise terms so as to indicate that the applicant had possession of these compounds at the time of filing of this application. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.).

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The 35 U.S.C. 103(a) rejection against claims 1-9 as being unpatentable over Bright et al. (a), Bright et al. (b), and further in view of Mahan et al., MacGregor et al., O'Toole et al., and Arrow et al. is maintained for reasons set forth in the Office Action mailed 7/18002 in Paper No. 7.

I. Applicant's arguments filed 12/23/02 in Paper No. 10 have been fully considered but they are not persuasive. Applicant's argument is three-fold. Applicants argue that first, the prior art reference or combination of references must teach or suggest all the claim limitations. Applicants argue that second, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings in order to arrive at the claimed invention. Applicants argue that third, there must be a reasonable expectation of success. This is not found persuasive because it would have been *prima facie* obvious for one of ordinary skill in the art to devise a method of screening for compounds that inhibit the virulence of *Pseudomonas* bacteria because bacteria such as *Pseudomonas* are responsible for serious infections leading to blindness and death. One of ordinary skill in the art would have been motivated to include the Crc locus because this gene is involved in the regulation of multiple catabolic pathways and may be important in the adaptive response of the organism to the milieu within the lung (see Bright et al. (b)).

As discussed in the previous Office Action, one of ordinary skill in the art would have been motivated to devise a method of screening for compounds that inhibit the virulence of *Pseudomonas* bacteria and detect the presence or absence of inhibition of the catabolite repression control (Crc) protein as recited in Claim 1 since the Crc protein locus is involved in the expression of *Pseudomonas aeruginosa* virulence factors (see Bright et al. (a) and Bright et al. (b)).

As discussed in the previous Office Action, one of ordinary skill in the art would have chosen a method of detecting the presence or absence of inhibition of Crc protein wherein the culture medium contains an amidase operon repressor and wherein the detection is carried out by detecting the poisoning of the bacteria by FAA and recited in claims 4-7 and had a reasonable expectation of success since the art has taught the identification of the Crc protein in various Crc mutant strains and FAA sensitivity as an assay of Crc function (see O'Toole et al.).

As discussed in the previous Office Action, it would have been obvious to one of ordinary skill in the art, at the time the invention was filed, to devise a method of screening for compounds that inhibit the virulence of *Pseudomonas* bacteria and detect the presence or absence of inhibition of the catabolite repression control (Crc) protein wherein the compound is an oligonucleotide as recited in Claims 7-8 and had a reasonable expectation of success since Arrow et al. have taught the use of oligonucleotides to inhibit the growth/virulence of bacteria.

Regarding the issue of the reasonable expectation of success, it is emphasized that the claimed method, as recited, has only 3 steps – providing culture media, adding a test compound, and detecting Crc protein inhibition. All these steps were routine at the time

of filing of the invention. Applicant has not provided any factual evidence to support their argument as to how an artisan would not have a reasonable expectation of success in performing the claimed method steps of the instant invention.

As discussed in the previous Office Action, the invention as a whole would therefore have been obvious to one or ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is (703) 306-3221. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 746-8693 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

tcg
March 10, 2003

RAM R. SHUKLA, PH.D
PATENT EXAMINER